

**Amendments to the Specification**

Please amend the corresponding paragraph bridging pages 34-35 as follows:

Antibody (supplied as a 2mg/ml stock solution) was used to coat the wells of microtiter plates at a 1:2,500 dilution in a 0.1M carbonate/bicarbonate buffer, pH 9.5. Pipetting of all reagents into microtiter wells was done with an 8-or 12- multichannel pipetter. The diluted antibody solution was pipetted into the wells of Nunc Maxisorp strip plates (100 microliters/well), then the plate strips was sealed in ~~Ziploc~~ ZIPLOC® plastic bags, and incubated overnight at room temperature (18-25°C). The next day, the coating solution was removed from each well by aspiration and 200 microliters of blocking buffer (5% sucrose, 5% Bovine serum albumin in phosphate buffered saline) was added to each well. Plate strips were placed back into ~~Ziploc~~ ZIPLOC® plastic bag and onto a benchtop rotator and rotated gently for 2 hours at room temperature. After the two hour blocking step, the contents of all wells were aspirated and the plate strips were placed upside down in a biosafety cabinet with the fan on, to dry for two hours. Dry plates were stored at 4°C until ready to use for the assay. Plates prepared in this manner are stable for at least ten weeks.

Please amend the corresponding paragraph located on page 50 as follows:

The remaining half of each organ sample was ground up in a 1.5 ml ~~Eppendorf~~ tube (EPPENDORF®), using a motorized pestle (Fisher brand) and the powdered sample was resuspended in a protein extraction buffer (50 mM Tris-HCl, pH 7.6, 1% Triton X-100, 150 mM NaCl, 2 mM PMSF, 10 mM EDTA, 20 mg/ml each aprotinin, leupeptin, and pepstatin A) and vortexed briefly to mix. The mixture was then centrifuged in a microfuge at 4°C for 15 minutes. The supernatant was transferred to a clean tube and the pellet was discarded. SDS-PAGE analysis was performed on the supernatants, followed by autoradiogram to analyze the pattern of radioactive protein in the tissue samples.

Please amend the corresponding paragraph located on page 73 as follows:

Western blot analysis was performed on Hfl-1 cells, A549 and Hec-1A and fibronectin cross-reactive species were detected with an anti-human fibronectin monoclonal antibody in

order to determine the endogenous expression of fibronectin. Whole cells were cultured (as described in Example 8), scraped from the flask and transferred to an ~~Eppendorf~~ a tube (EPPENDORF®). An equal volume of SDS-PAGE buffer (Novex) was added to each sample and mixed by vortexing. The samples were then heated for 10 minutes at 85°C and loaded onto a 10% Tris-glycine SDS-PAGE gel (Novex). Rainbow marker™ (Amersham) was run as the size standard. Blocking, probing, and washing were done as described in Example 8, except that a monoclonal anti-human fibronectin antibody was used as the primary antibody at a dilution of 1:2000 and a rabbit anti-mouse IgG-HRP conjugate was used as the secondary antibody at a dilution of 1:5,000.

Please amend the corresponding paragraphs bridging pages 74-75 as follows:

#### **MATRIGEL® Matrigel Invasion Assay with Fibronectin**

HMEC were grown in complete medium as described in the above wound healing assay. The assay was performed in serum-free medium. Cells (5000 per well) were incubated for 24 hours in Boyden chambers and tested for invasion through ~~Matrigel-coated filters~~ filters coated with a solubilized basement membrane preparation (MATRIGEL®) (Nucleopore). The bottom chamber medium contained VEGF (100 pg/ml) in all wells. The top chamber medium contained CC10 at the IC50 for migration inhibition (100 nM), plasma fibronectin (Sigma) at the same concentration (100 nM) or a combination of Fn and CC10. After 24 hours, attached but non-migrated cells were wiped off the upper face of each filter with ~~Q-tips~~ swabs (Q TIPS®) and migrated cells attached to the bottom face of each filter were stained and counted by two blinded observers. Data represent averages of four intermediate power fields (magnification x 100) counts plus or minus standard deviations. Data were analyzed by one-way ANOVA with Tukey correction for multiple comparisons

As shown in Figure 28, CC10 alone had no significant effect on Matrigel invasion in serum-free medium. Fn alone had a modest but statistically significant inhibitory effect. However, CC10 plus Fn inhibited invasion to a significantly higher extent than Fn alone or CC10 alone ( $p < 0.05$ ). Thus, CC10 requires the presence of Fn to inhibit solubilized basement membrane preparation (MATRIGEL®) ~~Matrigel~~ invasion by human primary microvascular endothelial cells. This is consistent with the observation that no saturable cell binding by CC10

was observed in the absence of Fn. These data indicate that CC10 binds HMEC as a complex with Fn and modulates Fn signaling. Qualitatively, the morphology of these cells incubated with Fn and CC10 together appeared in groups with intercellular adhesion. Cells incubated with Fn alone showed much less pronounced intercellular adhesion. Cells incubated in control medium or CC10 alone appeared mostly as individual cells. This suggests that upon binding Fn/CC10, cells modulate adhesion molecules and increase intercellular contacts, which may participate in the inhibitory effects observed.

Please amend the corresponding paragraph on page 77 as follows:

The anti-M-type PLA<sub>2</sub> receptor antisera and the anti-CD148 antisera were then used to analyze the crude extract and UG affinity-purified protein by Western blot. Equal volumes of crude lysates of Hfl-1 and UG affinity-purified proteins were run on 10% SDS-PAGE Tris-glycine gels (Invitrogen Corp.) with a ~~Rainbow~~ RAINBOW<sup>TM</sup> marker (Amersham Pharmacia, Corp.) using the manufacturers procedures. Gels were blotted to Hybond-P<sup>TM</sup> (Amersham Pharmacia, Corp.) using the Novex ~~Xcell~~<sup>TM</sup> XCELL II<sup>TM</sup> blotting apparatus according to instructions (Novex). The blots were blocked in 5% BSA (Sigma Co.) overnight at 4°C. Excess blocking solution was washed off with two washes in PBS with gentle shaking at room temperature. All following steps were performed at room temperature. Primary incubations with the rabbit antisera against the human M-type PLA<sub>2</sub> receptor and CD148 were done on separate blots containing identical protein samples. The blots were incubated in parallel with primary antisera dilutions of 1/500 in 5% BSA, 1X PBS, 0.2% Tween 20 for 1.5 hours at room temperature with gentle shaking. The primary antisera was then washed off with three washes in PBS, 0.1% Tween 20 with gentle shaking for 5-10 minutes each. Secondary incubations were goat anti-rabbit IgG conjugated to horse radish peroxidase (Pierce Chemical Co.) at 1/5000 in 5% BSA, 1X PBS, 0.1% Tween 20 for 1.5 hours at room temperature with gentle shaking. Three washes were then done in 1X PBS, 0.1% Tween 20 for 5-10 minutes each. The blots were developed using the ECL<sup>TM</sup> kit (Amersham Pharmacia Corp.) and viewed by autoradiography using Kodak ~~Biomax~~<sup>TM</sup> BIOMAX<sup>TM</sup> ML film.